COPERNICUS

2L SC ami + chemo in common *EGFR* NSCLC

COPERNICUS, a Pragmatic Phase 2b Study of Subcutaneous Amivantamab Plus Chemotherapy With Enhanced Dermatologic Adverse Event Prophylaxis in *EGFR*-Mutated Advanced NSCLC: Interim Results

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Background

- In MARIPOSA-2 (NCT04988295), 60% of participants with common *EGFR*-mutated advanced NSCLC interrupted IV amivantamab due to AEs, including IRRs and dermatologic AEs[1,2]
- Despite these interruptions, IV amivantamab in combination with carboplatin-pemetrexed chemotherapy significantly prolonged PFS vs chemotherapy[1]
  - Median blinded independent central review–assessed PFS was 6.3 vs 4.2 months (HR, 0.48; *P*<0.001)
  - Median INV PFS was 8.2 vs 4.2 months (HR, 0.41)
- Several studies have evaluated different approaches to improve treatment administration and the patient experience with amivantamab
  - In PALOMA-3 (NCT05388669) and PALOMA-2 (NCT05498428), SC amivantamab (co-formulated with recombinant human hyaluronidase PH20) reduced ARRs and treatment administration time (≤5 minutes vs 2–5 hours)[3,4]
    - Based on PALOMA, PALOMA-2, and PALOMA-3 data, SC amivantamab has been approved in several markets, including the US, Europe, Japan, and China[5–8]
  - In COCOON (NCT06120140), an enhanced prophylactic dermatologic regimen significantly reduced grade ≥2 dermatologic AEs vs standard of care (42% vs 75%; *P*<0.0001)[9]
- In COPERNICUS (NCT06667076), we present a protocol-specified interim analysis of SC amivantamab administered Q3W + chemotherapy on or after disease progression on an EGFR TKI in participants with common *EGFR*-mutated advanced NSCLC receiving enhanced dermatologic AE prophylaxis

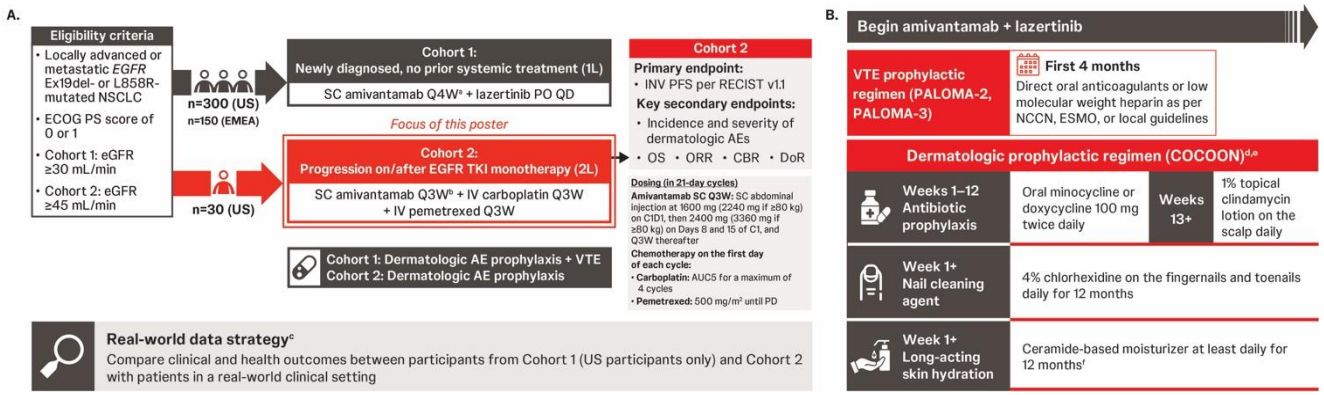
AE, adverse event; ARR, administration-related reaction; EGFR, epidermal growth factor receptor; HR, hazard ratio; INV, investigator-assessed; IRR, infusion-related reaction; IV, intravenous; NSCLC, non-small cell lung cancer; PFS, progression-free survival; Q3W, every 3 weeks; SC, subcutaneous; TKI, tyrosine kinase inhibitor.

1. Passaro A, et al. *Ann Oncol*. 2024;35(1):77–90. 2. RYBREVANT® (amivantamab-vmjw) injection, for intravenous use [package insert]. Janssen Biotech, Inc.; 2025. 3. Leighl NB, et al. *J Clin Oncol*. 2024;42(30):3593–3605. 4. Nadal E, et al. Presented at: European Society for Medical Oncology (ESMO) Congress; October 17–21, 2025; Berlin, Germany. 5. RYBREVANT FASPRO™ (amivantamab and hyaluronidase-lpuj) injection, for subcutaneous use [package insert]. Janssen Biotech, Inc.; 2026. 6. RYBREVANT® EPAR [product information]. Janssen-Cilag International NV; 2025. 7. RYBROFAZ® combination subcutaneous injection [package insert]. Janssen Pharmaceutical K.K.; 2025. 8. RYBREVANT FASPRO is for subcutaneous use only [package insert]. Janssen-Cilag AG; 2025. 9. Cho BC, et al. *J Thorac Oncol*. 2025;20(10):1517–1530.

Methods

- COPERNICUS is one of the largest studies enrolling in the US to evaluate common *EGFR*-mutated advanced NSCLC (**Figure 1A**)
- The pragmatic design included partnering with academic/community sites, reducing the stringency of inclusion criteria, and streamlining radiology requirements to mirror local practices in the US
- Participants received enhanced dermatologic prophylaxis aligned with the regimen described in COCOON (**Figure 1B**)
  - No prophylactic anticoagulation was required for Cohort 2
- The primary endpoint was INV PFS per RECIST v1.1, estimated using the Kaplan-Meier method
  - The null hypothesis was that the median INV PFS would be ≤4.5 months
- Safety and OS were key secondary endpoints
  - Safety included the incidence and severity of ARRs and dermatologic AEs

Figure 1: (A) COPERNICUS study design and (B) prophylaxis for dermatologic AEs[1]



- To further characterize these findings, a descriptive comparison with data from MARIPOSA-2 was included
- Safety and efficacy in the COPERNICUS study will continue to be evaluated as data mature

COPERNICUS (ClinicalTrials.gov Identifier: NCT06667076).
[a]In 28-day cycles until disease progression, withdrawal of consent, or the investigator decides to discontinue treatment, whichever comes first. [b]In 21-day cycles until disease progression, withdrawal of consent, or the investigator decides to discontinue treatment, whichever comes first. [c]The real-world comparison will be assessed under a separate protocol. [d]Prophylactic antibiotics: oral doxycycline or minocycline 100 mg BID and topical clindamycin lotion 1% on the scalp daily before bedtime. Paronychia prophylaxis: chlorhexidine 4% on the fingernails and toenails daily. Skin moisturization of the body and face at least daily. [e]Tacrolimus was added as a reactive management recommendation in COPERNICUS based on positive results from the COCOON treatment substudy.[2] In addition, a protocol amendment for COPERNICUS recommended zinc supplementation for participants with established zinc deficiency who experienced dermatologic AEs. [f]La Roche-Posay Lipikar AP+M moisturizer was used in COCOON.
1L, first-line; 2L, second-line; AE, adverse event; ARR, administration-related reaction; AUC, area under the curve; BID, twice daily; C, Cycle; CBR, clinical benefit rate; D, Day; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; eGFR, estimated glomerular filtration rate; EGFR, epidermal growth factor receptor; EMEA, Europe, the Middle East and Africa; ESMO, European Society for Medical Oncology; Ex19del, exon 19 deletion; INV, investigator-assessed; IV, intravenous; L858R, exon 21 L858R substitution; NCCN, National Comprehensive Cancer Network; NSCLC, non-small cell lung cancer; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PO, orally; Q3W, every 3 weeks; Q4W, every 4 weeks; QD, daily; RECIST, Response Evaluation Criteria in Solid Tumors; SC, subcutaneous; TKI, tyrosine kinase inhibitor; VTE, venous thromboembolism.
1. Cho BC, et al. *J Thorac Oncol*. 2025;20(10):1517–1530. 2. Spira AI, et al. Presented at: International Association for the Study of Lung Cancer (IASLC) | American Society of Clinical Oncology (ASCO) North America Conference on Lung Cancer (NACLC); December 5–7, 2025; Chicago, IL, USA.

Results: Baseline characteristics and PFS

Baseline demographic and clinical characteristics

- As of the clinical cutoff (March 16, 2026), Cohort 2 had completed enrollment with 29 participants in the US
  - Median (range) follow-up was 10.1 (0.5–12.7) months, and 69% of participants were still ongoing in the study
- The pragmatic design supported broad enrollment (**Table 1**)
  - Median age was 62 years, with 45% of participants ≥65 years of age and 21% ≥75 years of age
  - 38% were Asian, 7% were Black or African American, and 21% were Hispanic or Latino

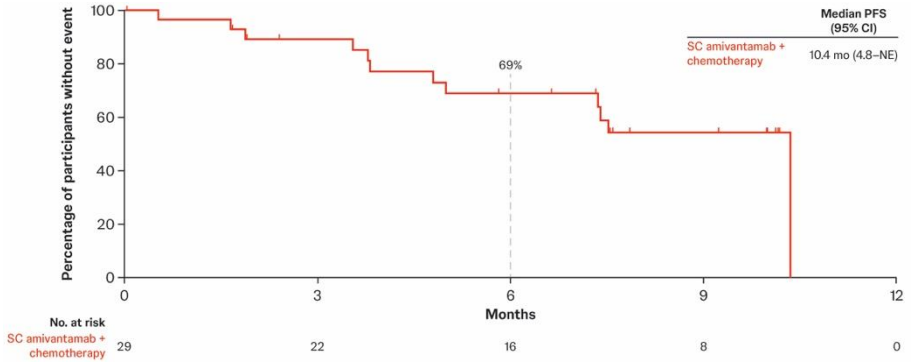
Efficacy

- The primary endpoint was met; median INV PFS was 10.4 months (95% CI, 4.8–NE; **Figure 2**)
- Median OS was immature at this time (NE [95% CI, 11.2–NE])

Table 1: Baseline demographic and clinical characteristics

Characteristic, n (%)	SC amivantamab Q3W + chemotherapy (n=29)
Median (range) age, years	62 (39–92)
Age ≥65 years	13 (45)
Age ≥75 years	6 (21)
Female	12 (41)
Race	
White	12 (41)
Asian	11 (38)
Black or African American	2 (7)
Other[a]	4 (14)
Hispanic or Latino	6 (21)
ECOG PS score	
0	11 (38)
1	18 (62)
History of smoking	10 (34)
Brain metastases	8 (28)
***EGFR* mutation type[b]**	
Ex19del	18 (62)
L858R	11 (38)

Figure 2: INV PFS



[a]Other includes unknown (7%) and not reported (7%). [b]Participants may have both Ex19del and L858R.
CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; Ex19del, exon 19 deletion; INV, investigator-assessed; L858R, exon 21 L858R substitution; NE, not estimable; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks; SC, subcutaneous.

Results: Safety

- Among all participants, INV ORR was 38% (95% CI, 21–58; **Figure 3**)
- CBR was 69% (95% CI, 49–85) and DCR was 83% (95% CI, 64–94)
- Among responders, median DoR was 5.6 months (95% CI, 2.8–NE), and in 18% of responses, duration was ≥6 months
- AEs were mostly grade 1 to 2, with no new safety signals identified (**Table 2**)
- 38% of participants interrupted amivantamab due to AEs; of those, 6 (21% of the total cohort) interrupted due to treatment-related AEs
- With enhanced dermatologic prophylaxis, rash (preferred term) incidence was 21% (none grade ≥3), showing numerical reductions versus MARIPOSA-2 (43% [grade ≥3, 6%])[1]
- No participants experienced ARR, showing a substantial reduction vs IRR observed in MARIPOSA-2 (58% [grade ≥3, 5%])[1]
- 2 participants experienced VTE (1 grade 2; 1 grade 3); 13 participants had VTE in MARIPOSA-2 (3 grade ≥3)[1]
- Grade ≥3 neutropenia was observed in 17% of participants, which is in line with what has previously been observed with carboplatin-pemetrexed use[2]; 2 participants interrupted amivantamab due to neutropenia

Figure 3: (A) Key secondary efficacy endpoints[a] and (B) best percentage (%) change in SoD of target lesions[b]

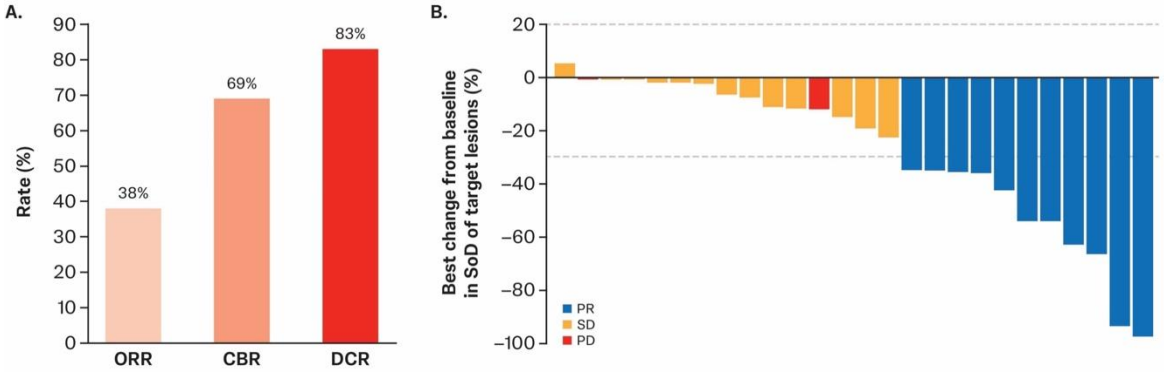


Table 2: TEAEs

TEAEs by preferred term (≥30%), n (%)	SC amivantamab Q3W + chemotherapy (n=29)	
	All grades	Grade ≥3
EGFR-related		
Fatigue	22 (76)	1 (3)
Dermatitis acneiform	11 (38)	2 (7)
Paronychia	9 (31)	0
MET-related		
Peripheral edema	9 (31)	0
Hypoalbuminemia	9 (31)	0
Chemotherapy-related		
Neutropenia	12 (41)	5 (17)
Leukopenia	11 (38)	5 (17)
Anemia	9 (31)	2 (7)
Thrombocytopenia	9 (31)	2 (7)
Other		
Nausea	16 (55)	1 (3)
Constipation	14 (48)	0
Decreased appetite	11 (38)	0
Hypokalemia	10 (34)	0

[a]ORR is defined as % of participants who achieved either a CR or PR using RECIST v1.1 as assessed by investigator. CBR is define as % of participants who achieved CR, PR, or durable SD of ≥11 weeks duration using RECIST v1.1 as assessed by investigator. DCR is defined as % of participants who achieved CR, PR or SD (regardless of durability of stabilization) using RECIST v1.1 as assessed by investigator. [b]3 response-evaluable participants with no evaluable target lesion measurements at any postbaseline disease evaluation assessments are not included in the plot.
AE, adverse event; ARR, administration-related reaction; CBR, clinical benefit rate; CI, confidence interval; CR, complete response; DCR, disease control rate; DoR, duration of response; EGFR, epidermal growth factor receptor; IRR, infusion-related reaction; NE, not estimable; ORR, overall response rate; PD, progressive disease; PR, partial response; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; SC, subcutaneous; SD, stable disease; SoD, sum of diameters; TEAE, treatment-emergent adverse event; VTE, venous thromboembolism.

1. Passaro A, et al. *Ann Oncol*. 2024;35(1):77–90. 2. Zhang L, et al. *Thoracic Cancer*. 2014;5(2014):50-56.

Conclusions

- The primary endpoint was met, with a median INV PFS of 10.4 months
- Enhanced dermatologic AE prophylaxis led to substantial reductions in dermatologic AEs and amivantamab interruptions, albeit with a different follow-up duration than in MARIPOSA-2[1]
- There were no ARRs observed with SC amivantamab

Key Takeaway

Early success was achieved at the planned interim analysis, demonstrating promising efficacy and improved safety for SC amivantamab Q3W + chemotherapy in participants with *EGFR*-mutated advanced NSCLC after disease progression on an EGFR TKI

AE, adverse event; ARR, administration-related reaction; EGFR, epidermal growth factor receptor; INV, investigator-assessed; NSCLC, non-small cell lung cancer; PFS, progression-free survival; Q3W, every 3 weeks; SC, subcutaneous; TKI, tyrosine kinase inhibitor.

1. Passaro A, et al. *Ann Oncol*. 2024;35(1):77–90.